

### REMARKS

Reconsideration is requested.

Claims 20 and 22-36 are pending. Claim 21 has been canceled, without prejudice. Claims 26-36 have been withdrawn from consideration.

The Examiner's indication that a certified copy of the priority document has not been received is not understood (see page 3 of the Office Action dated July 2, 2007) and clarification is requested in view of the contrary acknowledgement of receipt of the certified copy of the priority document noted in the Notice of Acceptance dated June 28, 2006. For completeness, the applicants note that as the present application is a 371 U.S. national phase of a PCT application, it would appear to be contrary to PCT Rule 17.2 for the Examiner to require the applicants to furnish a further certified copy of the priority document. Acknowledgement of receipt of the certified copy of the priority document by the Examiner is requested.

Regarding the Sequence Listing requirements, the specification has been amended to include the attached Sequence Listing, as further described below. The attached paper and computer readable copies of the Sequence Listing are the same. No new matter has been added.

With regard to the Examiner's interpretation of Figure 1, the applicants submit, with due respect, that the structural coordinates in Figure 1 do not teach an amino acid sequence within the definitions of the Sequence Listing Rules. The atom assignments are not to a linear amino acid sequence order. For example, the coordinates of Figure 1 are for a RAD51-BRC chimaera in which the RAD51 part of the chimaera is covalently bound to the BRC part by a polypeptide linker, but in Figure 1 the amino acids of the

linker are not in linear order with the amino acids of the RAD51 and BRC parts of the chimaera, so a SEQ ID based on the order of amino acid residues in column 4 of Figure 1 would give a sequence for the “wrong” protein. See the paragraph bridging pages 8 and 9 of the specification, which explains the layout of the table. Moreover, the table gives alternative side chain conformations for RAD51 amino acids 158, 208, 220, 326 and BRC repeat sequence amino acid 1519. Thus Figure 1 is a table of atomic coordinates - not a sequence to be listed in the a Sequence Listing as defined by the Patent Office Sequence Listing Rules. The atomic coordinate information content of the table would be essentially unchanged if column 4 mentioning the respective amino acid residues of the atoms was omitted from it entirely, i.e. that column is there purely for the convenience of the reader.

As for the Examiner’s comments relating to Figure 3, the specification has been revised to include the attached Sequence Listing which includes the Leu1521 to Glu1548 sequence of the Figure. The Examiner is requested to advise the undersigned in the event anything further is required in this regard relating to Figure 3.

With regard to the sequences of Figure 7(d), the specification was amended on page 5 in the Amendment filed January 3, 2007 to include a description of the sequence identifiers corresponding to the listed sequences.

With regard to the Examiner’s requirement for a sequence identifier relating to “The polypeptide of FHTA on page 5, line 11” (see page 4 of the Office Action dated July 2, 2007), page 5 of the specification was revised with the Amendment filed January 3, 2007 to identify the sequence as “amino acids 1-4 of SEQ ID NO:16”, as is believed

to be appropriate according to MPEP § 2422.03<sup>1</sup>. Clarification is requested in the event anything further is believed to be required with regard to this sequence.

With regard to the Examiner's requirement for a sequence identifier relating to "The polypeptide of "(ThrGlySer)4MetGly" on page 32, line2 [sic]", the Examiner is requested to see page 5 of the Amendment filed January 3, 2007, wherein the sequence identifier SEQ ID NO:14 was included in the specification to identify the sequence referred to by the Examiner. Clarification is requested in the event anything further is believed to be required with regard to this sequence.

The attached revised Sequence Listing includes the names of the listed inventors.

The statement that the attached paper and computer readable forms of the Sequence Listing are the same is found above. The statement that the paper and computer readable forms of the Sequence Listing filed January 3, 2007 are the same is found on page 12 of the Amendment filed January 3, 2007.

Withdrawal of the Examiner's objection to the specification based on the Sequence Listing requirements is requested.

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<sup>1</sup> 37 CFR 1.821(d) requires the use of the assigned sequence identifier in all instances where the description or claims of a patent application discuss sequences regardless of whether a given sequence is also embedded in the text of the description or claims of an application. This requirement is also intended to permit references, in both the description and claims, to sequences set forth in the "Sequence Listing" by the use of assigned sequence identifiers without repeating the sequence in the text of the description or claims. Sequence identifiers can also be used to discuss and/or claim parts or fragments of a properly presented sequence. For example, language such as "residues 14 to 243 of SEQ ID NO:23" is permissible and the fragment need not be separately presented in the "Sequence Listing." Where a sequence is embedded in the text of an application, it must be presented in a manner that complies with the requirements of the sequence rules. (Emphasis added.)

The title has been revised, as suggested by the Examiner. Withdrawal of the objection to the title is requested.

The Abstract has been revised as suggested by the Examiner. Withdrawal of the objection to the Abstract is requested.

The Examiner's comment regarding the inventorship is noted. See page 6 of the Office Action dated July 2, 2007. The Examiner is requested to see the Decision of June 13, 2006, in this regard. The Examiner is requested to indicate in a further Action if anything further is required by way of clarification.

The Section 112, second paragraph, rejection of claim 22 is believed to be obviated by the above amendments. The applicants believe that the ordinarily skilled person will appreciate the metes and bounds of the unamended claims and that the resolution becomes "better" as the resolution number decreases. Withdrawal of the Section 112, second paragraph, rejection of claim 22 is requested.

The Section 112, first paragraph "written description", rejection of claims 20-25 is traversed. The Section 112, first paragraph "enablement", rejection of claims 20-26 is traversed. Reconsideration and withdrawal of the rejections are requested in view of the above and the following comments.

Claim 20 is believed to address points (1), (2) and (3) in paragraph 3 on page 9 of the Office Action dated July 2, 2007.

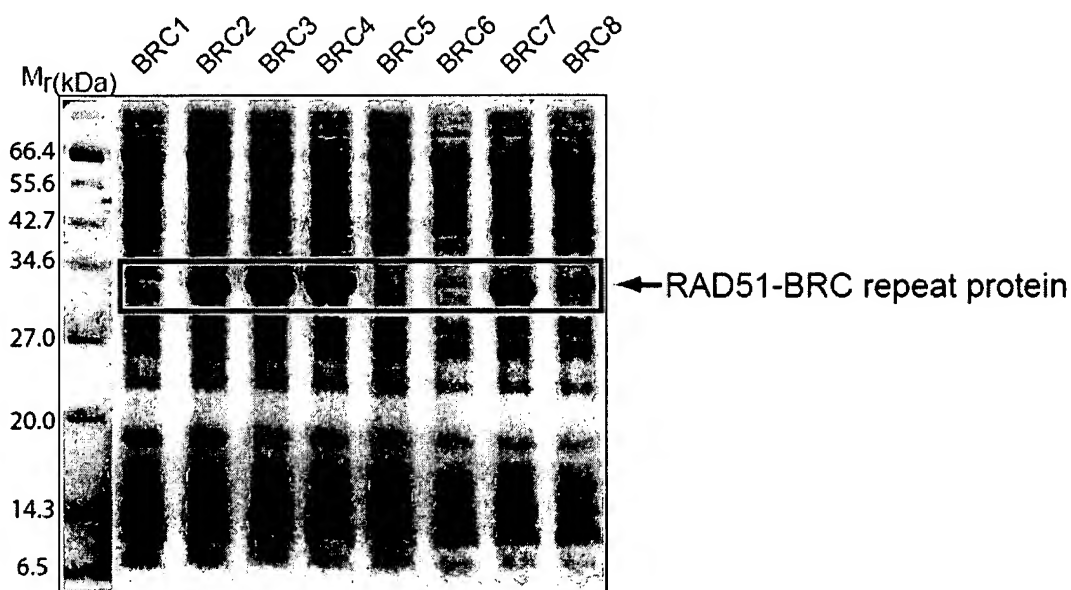
Regarding claims 24 and 25, the Examiner's citation of Liu et al (2002, Nucleic Acids Research, Vol. 30, pages 1009-1015) and Yuan et al. (1999, Cancer Research, Vol. 59, pages 3547-3551) as allegedly teaching that the claimed invention is in the

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public domain appears to be contrary to also asserting that the specification, in light of the prior art, fails to describe the claimed invention and/or that one of ordinary skill in the art would allegedly not have been able to make and use the claimed invention. The Examiner is requested to at least either withdraw the Section 112, first paragraph, rejections or withdraw the Section 102 rejections.

As for the description of joining of the two specific proteins, a detailed description is provided, for example, in the paragraph bridging pages 31 and 32 of the specification of the formation of a RAD51-BRC4 chimaera. There is no suggestion that other RAD51-BRC repeat sequence or RAD51 paralogue-BRC repeat sequence chimaeras cannot be formed in a similar way or that one of ordinary skill in the art would not appreciate that the applicants were in possession of the claimed invention at the time the application was filed.

Rather, the ordinarily skilled person would have had every expectation that other such chimaeras could be formed. As an example, one of the present inventors, in recently performed and as yet unpublished work, has shown that the technique of fusing BRC repeats (other than BRC4) to RAD51 creates not only chimaera proteins, but soluble chimaera proteins. Such soluble proteins represent the first step to obtaining crystals of RAD51-BRC repeat sequence complexes other than the particular complex described in the application. The gel below from this work is for different RAD51-BRC chimaera proteins produced in bacterial BL21(DE3) strain at 20°C. The gel shows that constructs encoding BRC repeats 2, 3, 4, 7 and 8 are strongly over-expressed in soluble form.



Therefore, the claims are submitted to be supported by an enabling disclosure which will also lead one of ordinary skill to conclude that the applicants were in possession of the claimed invention at the time the application was filed.

The Section 101 rejection of claims 24 and 25 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

Specifically, the Examiner is requested to appreciate that RAD51-BRC repeat sequence chimaera proteins and RAD51 paralogue-BRC repeat sequence chimaera proteins are not naturally occurring products. In nature, RAD51 or RAD51 paralogue is one protein and BRCA2 (or a different protein with a BRC repeat) is another separate protein. The specification at page 6 line 10 to page 7 line 14 and in the paragraph bridging pages 31 and 32 describes how the present inventors covalently bound RAD51 to a BRC repeat sequence to produce an artificial chimarea that could be crystallised for X-ray structural analysis. Therefore, the Examiner's suggestion to insert "isolated" or "purified" is believed to be unnecessary.

Withdrawal of the Section 101 rejection is requested.

The Section 102 rejection of claims 20-25 over Pellegrini (21 November 2002, Nature, Vol. 420, pages 287-293), is traversed. The Section 102 rejection of claim 24 over Liu (2002, Nucleic Acids Research, Vol. 30, pages 1009-1015), is traversed. The Section 102 rejection of claim 25 over Yuan (1999, Cancer Research, Vol. 59, pages 3547-3551), is traversed. Reconsideration and withdrawal of the Section 102 rejections are requested in view of the above and the following distinguishing comments.

Pellegrini et al. is believed to have published on 21 November 2002. The present application has a priority date of 14 October 2002. A certified copy of the priority document has been received by the Patent Office according to the Notice of Acceptance mailed June 28, 2006. Pellegrini et al. is not believed to be citable prior art. Withdrawal of the Section 102 rejection based on Pellegrini et al. is requested.

With regard to Liu, the Examiner is understood to suggest that the dipeptide IleIle of the HA protein of Liu et al. is encompassed by the term "BRC repeat sequence" of claim 24. While the applicants disagree with the Examiner's interpretation, claim 24 has been revised without prejudice to require that the BRC repeat sequence contains the seven residue sequence (F or Y)x(T or S)A(S or H or G)(G or S or N)(K or R or T) where x can be any residue. Basis for this amendment can be found, for example, at page 38 lines 5-6, which states "[r]esidues 1524-FHTASGK-1530, with the exception of His1525, form a contiguous block of highly conserved amino acids"; the consensus sequence at the foot of Figure 3 which shows the sequence Fx(T or S)AS(G or S or N)K; and the table of Figure 3 itself which indicates that Y can be an alternative for F1524, H or G can be alternatives for S1528, and R or T can be alternatives for K1530.

The HA protein of Liu et al. does not include such a sequence, and thus claim 24 is submitted to be novel over Liu et al.

As to claim 25 and Yuan, the basis of the Examiner's objection is not completely understood as the Examiner appears to suggest that GFP protein of Yuan et al. is encompassed by the requirement in claim 25 for a BRC repeat sequence. It is not clear which part of the BRC-GFP protein the Examiner believes anticipates the requirement in claim 25 for a RAD51 paralogue. Nonetheless, claim 25, like claim 24, requires that the BRC repeat sequence contains the residue sequence (F or Y)x(T or S)A(S or H or G)(G or S or N)(K or R or T) where x can be any residue. Further claim 25 requires that the RAD51 paralogue has at least 15% sequence identity with RAD51 in the RecA homology domain (basis is at e.g. page 14 lines 15-20 of the specification). Accordingly, even if the BRC repeat of Yuan et al. contains the residue sequence (F or Y)x(T or S)A(S or H or G)(G or S or N)(K or R or T), the GFP does not have at least 15% sequence identity with RAD51 in the RecA homology domain. Therefore claim 25 is novel over Yuan et al.

Withdrawal of the Section 102 rejections is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required in this regard.



VENKITARAMAN et al.  
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Amendment

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By:                     /B. J. Sadoff/                      
                    B. J. Sadoff  
                    Reg. No. 36,663

BJS:  
901 North Glebe Road, 11th Floor  
Arlington, VA 22203-1808  
Telephone: (703) 816-4000  
Facsimile: (703) 816-4100